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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/470,667	12/22/1999	AKIRA ASAKURA	13735(109700	6424

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/470,667

Applicant(s)

ASAKURA ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13-24 and 36 is/are pending in the application.
- 4a) Of the above claim(s) 1-3, 9 and 17-28 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4-8, 10, 11, 29 and 33 is/are allowed.
- 6) ☒ Claim(s) 13, 14-16, 30-32, 34 and 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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Response to Office Action including Amendment and Petition for Extension of time, filed on December 9, 2002 as paper No. 19, is acknowledged. The amendments to the claim and specification have been entered as requested. Claim 12 and 35 are cancelled. Claims 4, 5, 10, 11, 29, 30 and 31 have been amended. Claims 1-11, 13-34 and 36 are pending in the application. Claims 4-8, 10-16 and 29-334 and 36 are the subject of this Office Action. Claims 1-3, 9, and 17-28 are withdrawn from consideration as drawn to the non-elected invention.

Detailed Office Action

1. Sequence listing

Corrected sequence listing, computer readable form, the first and second declaration under C. F. R. §1.132 by Masako Shinjoh, declaration under C. F. R. §1.132 by Yoshita Murata, and declaration under C. F. R. §1.132 by Masao Mashita are acknowledged.

The corrected sequence listing has been entered.

2. Rejections withdrawal

2.1. 35 U.S.C. 101

Rejection of claim 4 and 5 under 35 U.S.C. 101 made in the previous Office Action, paper 16, is withdrawn because the claims have been amended.

2.2. 35 U.S.C., section 112, second paragraph

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Rejection of claim 30 made is rejected under 35 U.S.C. 112, second paragraph, made in the previous because Office Action, paper 16, is withdrawn because the claim has been amended and is not indefinite any more.

2.3. 35 U.S.C. section 112, first paragraph

2.3.1 Lack of written description

Rejection of claim 8 and 33 under 35 U.S.C. 112, first paragraph, made in the previous because Office Action, paper 16, is withdrawn because Applicants provided the evidence of biological deposit of the pSSA102R vector under the terms of the Budapest Treaty and the statement that all restriction imposed by the depositor on the availability of the deposit to the public will be irrevocably removed upon the granting of the patent.

Rejection of claim 29 under 35 U.S.C. 112, first paragraph, made in the previous Office Action, paper 16, is withdrawn because the claim has been amended.

2.3.2. Scope of enablement

Rejection of claims 10-11 under this paragraph made in the previous because Office Action, paper 16, is withdrawn because the claims have been amended.

Rejection of claim 29 under this paragraph made in the previous because Office Action, paper 16, is withdrawn because the claims have been amended.

3. Rejections

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3.1. 35 U.S.C. 112, second paragraph

Claim 36 recites the limitation "a recombinant organism according to claim 11" in the first line. There is insufficient antecedent basis for this limitation in the claim, because claim 11 is not directed to "a recombinant organism".

3.2. 35 U.S.C. section 112, first paragraph

3.2.1 Lack of written description

Claims 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a large and variable genus of DNA molecules comprising a polynucleotide sequence encoding a polypeptide fragment consisting of amino acid residues 1-95/1-135 of SEQ ID NO: 5. Neither the claims nor the specification discloses the function of such DNA molecules with exception of SEQ ID NO: 1 encoding AADH enzyme of *Gluconobacter oxydans* and some DNA molecules encoding hybrid enzymes. The function of fragments consisting of 1-95/1-135 amino acid residues of SEQ ID NO: 5 is to be used in a hybrid enzymes and the function of polynucleotide sequences encoding the fragments consisting of residues 1-95 and 1-135 is to be used in hybrid genes encoding said hybrid enzymes. However, the function of other species of the claimed genus, i.e., any isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide fragment consisting of amino acid

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residues 1-95 or 1-35 of SEQ ID NO: 5 is not recited by claims or set forth in the specification.

The genus of nucleic acid molecules claimed is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only several species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 34 is included in this rejection because it depends on any of the rejected claims.

3.2.2. *Scope of enablement*

Claims 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA molecule of SEQ ID NO: 1 encoding SEQ ID NO: 5 having the AADH activity, or for some DNA molecules encoding hybrid enzymes having AADH activity, as described on page 60 of the specification, does not reasonably provide enablement for any polynucleotide comprising an nucleotide

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sequence encoding polypeptides consisting of 1-95 or 1-135 of SEQ ID NO:5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are so broad as to encompass any DNA, from any natural and man-made source, wherein said DNA encodes the amino acid sequence that consists of amino acid residues 1-95 or 1-135 of SEQ ID NO: 5. Thus, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA molecules broadly encompassed by the claims. The specification provides for SEQ ID NO: 1 encoding SEQ ID NO: 5 having the AADH activity, and some hybrid DNA molecules containing fragments encoding 1-95 or 1-135 of SEQ ID NO: 5.

While engineering and expressing genes, as well as measuring enzymatic activities of the encoded proteins are well developed and skills of artisans high, it is not routine in the art to use all DNA libraries, from natural and man-made sources, to modify the DNA molecules so that they comprise nucleotide sequences encoding amino acid residues 1-95, or 1-135, express said DNA molecules, isolate the proteins, measure their enzymatic activity and select the ones having desired AADH activity. The specification does not support the broad scope of the claims that encompass extremely large number of DNA molecules. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broad claims. The scope of the

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claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination which of DNAs will encode a polypeptide retaining the AADH activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 34 is included in this rejection as dependent from any of claims 30 and 31.

4. New rejections

4.1. 35 U.S.C. 101

Claims 16 and 36 are rejected as directed to non-statutory subject matter. The claims are directed to any recombinant organism, including human recombinant organism. Therefore, the claims are directed to non-statutory subject matter.

3.2. 35 U.S.C. 112, second paragraph

Claims 13-15 recite the limitation "a recombinant organism according to claim 10" in the first line. There is insufficient antecedent basis for this limitation in the claim, because claim 10 is not directed to "a recombinant organism".

Claim 32 recites the limitation "a recombinant organism according to claim 11" in the first line. There is insufficient antecedent basis for this limitation in the claim, because claim 11 is not directed to "a recombinant organism".

Claim 32 is confusing as containing improper Markush group. The claim recites the Markush group of fragments of SEQ ID NO: 5, however combinations of fragments

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of SEQ ID NO: 5 and other amino acid sequences are included in this group. These combinations are not fragments of SEQ ID NO:5.

4.3. 35 U.S.C. section 112, first paragraph

4.3.1. Lack of written description

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is directed to a genus of nucleic acids encoding a polypeptide containing a fragment of SEQ ID NO: 5 with alcohol and aldehyde dehydrogenase activity, the fragment of SEQ ID NO: 5 being selected from the group consisting of (a) amino acid residues 1-95, (b) amino acid residues 1-125, (c) amino acid residues 1-128, (d) amino acid residues 1-135, (e) amino acid residues 180-556, combinations of (a) with (e), combinations of (b) with (e), combinations of (c) with (e) and combinations of (d) with (e).

The specification does not contain disclosure of the structure of all nucleic acid sequences included in the claimed genus. The genus of nucleic acids claimed is a large variable genus with the potentiality of encoding many different proteins. Therefore, many structurally distinct nucleic acids are encompassed within the scope of these claims. The specification discloses only a few species of the claimed genus, i.e., that of SEQ ID NO: 1 encoding SEQ ID NO: 5 and chimera species explicitly described

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on page 59, line 6 and further. This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Applicant did not disclose that the residues 1-95, 1-125, 1-128 and 1-135 of SEQ ID NO: 5 have the activity of alcohol and aldehyde dehydrogenase. A sufficient written description of a genus of DNA molecules may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, **which features constitute a substantial portion of the genus**. The recited structural feature of the genus (i.e., encode a polypeptide comprising a fragment of SEQ ID NO: 5 being selected from the group consisting of (a) amino acid residues 1-95, (b) amino acid residues 1-125, (c) amino acid residues 1-128, (d) amino acid residues 1-135, (e) amino acid residues 180-556, combinations of (a) with (e), combinations of (b) with (e), combinations of (c) with (e) and combinations of (d) with (e), does not constitute a substantial portion of the genus as the remainder of the structure of any nucleic acid encoding a polypeptide having the feature recited by the claim (i.e., an alcohol or aldehyde dehydrogenase) is completely undefined and the specification does not define the remaining structural features necessary for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

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Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 34 is included in this rejection as dependent from claim 32.

3.3. Scope of enablement

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA molecule of SEQ ID NO: 1 encoding SEQ ID NO: 5, or chimeras characterized structurally on page 59 of the specification, having the AADH activity, does not reasonably provide enablement for DNA encoding a polypeptide containing a fragment of SEQ ID NO: 5 with alcohol and aldehyde dehydrogenase activity, the fragment of SEQ ID NO: 5 being selected from the group consisting of (a) amino acid residues 1-95, (b) amino acid residues 1-125, (c) amino acid residues 1-128, (d) amino acid residues 1-135, (e) amino acid residues 180-556, combinations of (a) with (e), combinations of (b) with (e), combinations of (c) with (e) and combinations of and combinations of (d)with (e).

The claim is so broad as to encompass any engineered or natural DNA molecule that encodes a polypeptide containing a fragment of SEQ ID NO: 5 with alcohol and aldehyde dehydrogenase activity, the fragment of SEQ ID NO: 5 being selected from the group consisting of (a) amino acid residues 1-95, (b) amino acid residues 1-125, (c) amino acid residues 1-128, (d) amino acid residues 1-135, (e) amino acid residues 180-

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556, combinations of (a) with (e), combinations of (b) with (e), combinations of (c) with (e) and combinations of and combinations of (d)with (e).

The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA molecules broadly encompassed by the claims. The specification provides for SEQ ID NO: 1 encoding the AADH of SEQ ID NO: 5 and enzymatically active chimeras explicitly described on page 59.

Applicant, however, does not guide how to construct polynucleotides encoding at least a fragment of SEQ ID NO: 5 comprising amino acid residues (a) 1-95, or (b) 1-125, or (c) 1-128, or (d) 1-135, or (e) d 180-556, wherein said polynucleotides encode alcohol and aldehyde dehydrogenase activity. Applicant also does not instruct how to make a polynucleotide encoding any combination of (a) and (e), (b) and (e), (c) and (e) and (d) and (e) so that said polynucleotide encoded alcohol and aldehyde dehydrogenase activity. Thus, the guidance on the part of Applicant is insufficient. Without a further guidance as to the detailed structure of the claimed polynucleotides the result of making of the claimed invention is unpredictable. One skilled in the art realizes that even a single change of codon leading to one amino acid change in an enzyme sequence may turn the protein inactive, thus, the claimed invention encompasses many DNA molecules that do not encode for the AADH activity.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination which of DNAs will encode a polypeptide retaining the AADH activity is

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unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 34 is included in this rejection as dependent from claim 32.

4. Conclusion

Claims 4-8, 10-11, 29 and 33 are allowed for reasons indicated in the previous Office Action, paper no. 13.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Patent Examiner

Rebecca E. Prouty
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